Cardiac Amyloidosis Mimicking Hypertrophic Cardiomyopathy With Obstruction: Treatment With Disopyramide

Anthony A. Philippakis, MD, PhD; Rodney H. Falk, MD

A 71-year-old man presented with 4 posturally related syncopal episodes. He carried a diagnosis of asymptomatic hypertrophic cardiomyopathy (HCM) without obstruction based on an echocardiogram 7 years earlier. Echocardiography at the time of syncope evaluation demonstrated a hyperdynamic left ventricle with a septal thickness of $\approx 20$ mm (an increase of 4 mm from an earlier echocardiogram), newly present systolic anterior motion of the mitral valve, and a peak left ventricular (LV) outflow tract gradient of 42 mm Hg at rest and 120 mm Hg with Valsalva maneuver (Figure 1). He was referred for septal myectomy, and cardiac catheterization demonstrated nonobstructive coronary artery disease. An ECG showed low-voltage limb leads, unusual in HCM (Figure 2), and cardiac magnetic resonance imaging (MRI) revealed delayed gadolinium enhancement in the papillary muscles, transmural enhancement involving the basal lateral walls, and subendocardial enhancement of the basal, mid, and distal anterior walls. There was also extensive gadolinium uptake in the atrial walls (Figure 3). Because the cardiac MRI suggested an infiltrative process, a cardiac biopsy was performed. This demonstrated extensive amyloid infiltration (Figure 4). Immunohistochemistry was positive for transthyretin, but negative for amyloid A and $\kappa/\lambda$ light chains. Genetic testing for common mutations associated with HCM was negative, and no transthyretin mutations were detected. A diagnosis of wild-type transthyretin cardiac amyloidosis (senile systemic amyloidosis) mimicking HCM with obstruction was made.1

In light of the diagnosis of cardiac amyloidosis, the risk of surgical myectomy was considered to be increased, with an unknown risk-benefit ratio, and alcohol septal ablation was thought unlikely to be successful. Based on disopyramide’s efficacy in reducing LV outflow tract gradient in HCM with obstruction,2 a trial of a single dose of disopyramide 300 mg was instituted under carefully monitored conditions. This resulted in a decrease in the murmur and a reduction in the peak LV outflow tract gradient, from 40/120 mm Hg at rest and Valsalva maneuver, respectively, to 6/10 mm Hg 1 hour after drug administration (Figure 5). He was continued on short-acting disopyramide 200 mg 3 times daily; the gradient

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Figure 1. Baseline imaging of the patient. Left, A 4-chamber view of the heart pretreatment. Although there was general thickening of the left ventricle, this was most marked in the ventricular septum. Right, M-mode imaging in the parasternal long-axis view at the level of the mitral valve. The arrow shows apposition of the mitral valve leaflet to the septum during systole. (This was well seen on the real-time 2-dimensional image, but difficult to visualize on a “freeze-frame” of the 2-dimensional image.)
remained reduced, and he had an improvement in well-being, characterized by decreased dyspnea in exertion and resolution of syncopal episodes. In contrast to LV ejection fraction, which did not change appreciably, longitudinal strain imaging with tissue Doppler speckle tracking showed a marked decrease in LV strain after chronic disopyramide use in comparison with pretherapy (Figure 6).

Cardiac amyloidosis is an infiltrative cardiomyopathy characterized by concentric left and right ventricular thickening. Occasionally, asymmetrical septal infiltration occurs mimicking HCM, and several cases of LV outflow tract obstruction have been reported. In the case presented, the suspicion that this was not typical HCM was raised by the appearance of the distribution of the delayed gadolinium enhancement cardiac MRI, in particular, the uptake of gadolinium in the atria. To our knowledge, this is the first reported case of a patient with cardiac amyloidosis and outflow tract obstruction in whom the obstruction was successfully treated with disopyramide. Although the possibility that the patient has HCM in addition to amyloidosis cannot be completely ruled out, we believe this to be unlikely given the progressive nature of the disease after its recognition relatively late in life and the MRI and electrocardiographic appearance. The persistence of an ejection fraction >70% following chronic disopyramide use is consistent with the modest decrease in this parameter noted by other investigators. Although the LV ejection fraction did not appear to change after disopyramide, there was a 45% decrease in longitudinal 4-chamber strain (from −14.5% to −8%) and a similar decrease in systolic strain rate. This may indicate that the longitudinal fibers are more sensitive to the negative inotropic effects of disopyramide, or it may simply indicate that speckle strain imaging is a more easily measurable marker of systolic LV function.

This case illustrates the importance of multimodality imaging and of a willingness to consider an alternative diagnosis even when the initial pathology seems clear. Extrapolation of therapy from 1 disease (HCM) to another (cardiac amyloidosis), based on the pathophysiology, produced a positive outcome, and the recent technique of tissue Doppler speckle strain provided insights into the mechanism of improvement.

Disclosures
None.

References
Figure 3. Delayed enhancement cardiac MRI images. A, Two-chamber view. There are foci of subendocardial enhancement in the anterior wall and extensive midwall enhancement in the inferior wall. Note also the marked enhancement of the left atrium. B, Short-axis image at the midventricular level showing diffuse, near-circumferential, subendocardial late enhancement of the left ventricle, and right ventricle, as well. These features are strongly suggestive of cardiac amyloidosis and would be very unusual in hypertrophic cardiomyopathy. MRI indicates magnetic resonance imaging.

Figure 4. Histology of cardiac biopsy on hematoxylin and eosin staining (top) and sulfated Alcian blue (bottom). On hematoxylin and eosin stain, the amyloid is the amorphous light-pink material between myocytes. On sulfated Alcian blue staining, myocytes stain yellow, and amyloid is turquoise-blue.
Figure 5. Peak left ventricular outflow tract gradient Doppler echocardiography at baseline and at rest (A), at baseline with Valsalva (B), after disopyramide at rest (C), and after disopyramide with Valsalva (D).

Figure 6. Doppler speckle tracking showing baseline strain characteristics (A) and a marked decrease in left ventricular strain after disopyramide, as well (B). The dotted line in each image denotes an average across ventricular positions; the arrow points to the nadir of these curves that is used for quantification of peak strain. Individual colored lines represent regional segmental strain. The apical strain is least impaired, a finding commonly seen in cardiac amyloidosis.
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